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published in

Muscle and Nerve
1999

DOI (link to publisher)

[10.1002/\(SICI\)1097-4598\(199909\)22:9<1249::AID-MUS13>3.0.CO;2-N](https://doi.org/10.1002/(SICI)1097-4598(199909)22:9<1249::AID-MUS13>3.0.CO;2-N)

document version

Publisher's PDF, also known as Version of record

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citation for published version (APA)

Gerrits, H. L., de Haan, A., Hopman, M. T. E., van der Woude, L. H. V., Jones, D. A., & Sargeant, A. J. (1999). Contractile properties of the quadriceps muscle in individuals with spinal cord injury. *Muscle and Nerve*, 22, 1249-1256. [https://doi.org/10.1002/\(SICI\)1097-4598\(199909\)22:9<1249::AID-MUS13>3.0.CO;2-N](https://doi.org/10.1002/(SICI)1097-4598(199909)22:9<1249::AID-MUS13>3.0.CO;2-N)

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ABSTRACT: Selected contractile properties and fatigability of the quadriceps muscle were studied in seven spinal cord-injured (SCI) and 13 able-bodied control (control) individuals. The SCI muscles demonstrated faster rates of contraction and relaxation than did control muscles and extremely large force oscillation amplitudes in the 10-Hz signal ($65 \pm 22\%$ in SCI versus $23 \pm 8\%$ in controls). In addition, force loss and slowing of relaxation following repeated fatiguing contractions were greater in SCI compared with controls. The faster contractile properties and greater fatigability of the SCI muscles are in agreement with a characteristic predominance of fast glycolytic muscle fibers. Unexpectedly, the SCI muscles exhibited a force–frequency relationship shifted to the left, most likely as the result of relatively large twitch amplitudes. The results indicate that the contractile properties of large human locomotory muscles can be characterized using the approach described and that the transformation to faster properties consequent upon changes in contractile protein expression following SCI can be assessed. These measurements may be useful to optimize stimulation characteristics for functional electrical stimulation and to monitor training effects induced by electrical stimulation during rehabilitation of paralyzed muscles.

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CONTRACTILE PROPERTIES OF THE QUADRICEPS MUSCLE IN INDIVIDUALS WITH SPINAL CORD INJURY

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Accepted 11 May 1999

A spinal cord injury (SCI) leads to significant muscular changes below the level of the spinal lesion. One of the most distinct phenomena is a marked decrease in muscle mass as a result of disuse consequent upon the interruption of descending spinal motor pathways.¹⁰ In addition, a dramatic change in muscle fiber composition has been reported, whereby slow oxidative, high-endurance, type I muscle fibers are converted to fast glycolytic, highly fatigable, type II muscle fibers in animal^{17,20} as well

as in human skeletal muscle.^{5,11,19,25,27} Consequently, the usually heterogeneous human muscle composed of similar amounts of type I and type II fibers⁸ shifts towards a homogeneous muscle composed of predominantly type II fibers, which is associated with a marked increase in fatigability.^{10,31} It is believed that the changes in the expression of contractile protein, most notably of myosin heavy chain isoforms, lead to concomitant changes in contractile speed towards those of fast muscle. A number of studies have provided evidence for the development of faster contractile properties following spinal cord transection in animals,^{7,18,20} and similar results have been reported in related papers describing human SCI research. However, with respect to physiological properties, data are usually restricted to small, distally located muscles such as the tibialis anterior^{26,33} or the soleus muscle.^{29,30} It is probably of greater

Abbreviations: $\frac{1}{2}$ Rt, half relaxation time; FOA, force oscillation amplitude relative to the mean force; MFR, maximal rate of force rise; MSC, maximal stimulated contraction; MVC, maximal voluntary contraction; SCI, spinal cord injury

Key words: contractile properties; electrical stimulation; fatigue; quadriceps muscle; spinal cord injury

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CCC 0148-639X/99/091249-08
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importance to assess the changes in the contractile properties of the larger, more proximally located quadriceps muscle, because weakness and fatigability of these knee extensors limit the optimal use of rehabilitation programs using functional electrical stimulation to achieve standing and walking.¹⁵

The purpose of the present study was to investigate and characterize the contractile properties of the quadriceps muscle in people with SCI compared with those of able-bodied individuals. This was accomplished by examining selected contractile speed characteristics and force–frequency relationships as well as fatigability in response to repeated electrical activation.

METHODS

Subjects. Seven SCI subjects (age, 22–46 years; six men and one woman) and 13 able-bodied control subjects (age, 21–35 years; six men and seven women) participated in this study. Mean height and weight were 182 ± 10 cm and 78 ± 11 kg, respectively, in the SCI group and 173 ± 11 cm and 67 ± 11 kg, respectively, in the control group. The characteristics of the SCI subjects with respect to the lesion are presented in Table 1. Spinal reflexes were present in all SCI subjects. None of the subjects had a previous history of neurological disorder or fractures of the lower limbs. Control subjects were all moderately active physically. All subjects gave written informed consent after a careful explanation of the methodology and testing procedures. This study was approved by the Medical Ethical Committee of the University of Nijmegen.

Procedure. Electrically stimulated isometric quadriceps contractions were obtained while subjects were seated on a specially developed chair with a

knee angle of 120° and hip angle of 100° . This corresponds with the optimal position for maximal electrically evoked isometric force in healthy²⁸ and in SCI^{16,24} subjects. To minimize movement of the leg during the measurements, the pelvis and upper thigh were securely fixed to the seat. A nonextensible strap was placed around the distal part of the tibia and mounted to a (strain gauge) force transducer, which was allowed to rotate in order to assure a force direction perpendicular to the leg (Fig. 1). The force signal was amplified (strain indicator type CA660, Peekel Instruments, Rotterdam, The Netherlands), digitized with 1000-Hz sample frequency, and stored on hard disk for off-line analysis.

Tests were conducted under standard conditions, with room temperature kept constant at 24°C , and subjects were in the room for at least 45 min before the actual testing protocol started.

Electrical Stimulation. Electrical pulses were delivered to the quadriceps muscle through two surface electrodes (10×13 cm, Electro-Medical Supplies, Greenham Ltd, Wantage, Oxfordshire, UK). The electrodes were placed over the distal and proximal part of the anterior thigh after the skin was scrubbed with alcohol. A personal computer running a custom-made software program controlled the frequency and number of square-wave pulses (0.20 ms duration) delivered by a constant-current, high-voltage stimulator (model DS7A, Digitimer Ltd, Hertfordshire, UK).

Protocol. During the electrical stimulation, we aimed to stimulate at least 30% of the muscle mass to ensure that a representative part of the muscle was activated. In the control subjects, this was obtained by asking subjects to perform three maximal volun-

Table 1. Characteristics of SCI subjects with respect to the level of the spinal lesion, completeness of the lesion, and duration of the lesion.

SCI subject	Level of spinal lesion	ASIA class*	Time since injury (yr)
1	C5	B	4
2	T4	A	1
3	C5	A	15
4	C5	C	21
5	T5	A	1
6	C7	A	15
7	C5	B	10

*ASIA (American Spinal Injury Association, 1992) score is used to classify the completeness of the lesion: A, sensory and motor complete; B, sensory incomplete but motor complete; C, sensory and motor incomplete but no functional motor activity.

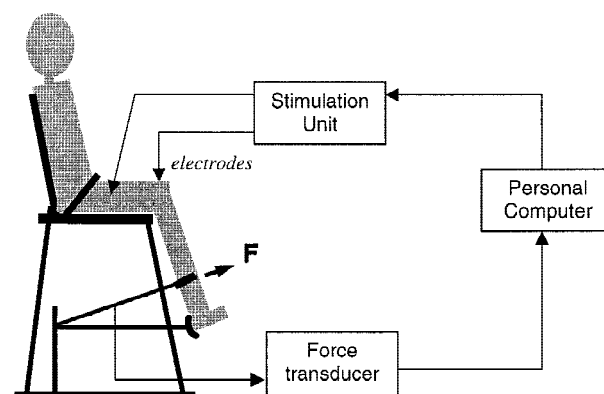


FIGURE 1. Schematic representation of the experimental set-up. F represents the isometric force produced by the knee extensor muscles after stimulation.

tary knee extensions of approximately 3 s duration, with 1 min rest between contractions. The highest of three repetitions was taken as the maximal voluntary contraction (MVC) force. Subsequently, electrical bursts (20 Hz) of 1 s duration were delivered to the muscle with increasing current until 30% of MVC was reached. In the SCI individuals, the determination of MVC was not possible because of loss of voluntary control. As an alternative, we delivered electrical stimuli in repeated bursts (20 Hz) of 1 s duration, increasing the current stepwise until the force started to level off.

At that point, it is assumed that the entire muscle was activated. A stimulation frequency of 20 Hz was used in order to avoid high forces and minimize the consequent risk to muscle tendon or bone. From the plot of force against current, we determined the current required to generate 30% of the maximal stimulated contraction (MSC) force. In both experimental groups, the current was kept constant at the level corresponding with the 30% MVC or MSC value during the remainder of the test procedure.

Frequency Response. A force–frequency relationship was obtained from electrical stimulation by 10 bursts of 1 s duration, ranging from 10 to 100 Hz. Bursts were applied in randomized order and separated by 1 min rest.

Fatigue. The resistance to fatigue was assessed by activating the quadriceps muscle repetitively using 30 Hz bursts of 1 s duration every 2 s (on:off time = 1 s:1 s), until force declined to 30% of the prefatigue value. The maximum stimulation time was set at 10 min.

Analysis of Variables. Off-line analysis of force records was performed using custom-made software programs. Peak forces were defined at each stimulation frequency. The stimulus frequency required to generate half the maximal tetanic 100-Hz force was determined for each subject by interpolation from the force–frequency relationship. In addition, the ratio of forces generated by 20-Hz and 50-Hz stimulation (20/50 ratio) was calculated.

Contraction and relaxation rates of isometric tetani were calculated as indices of muscle speed. Normalized maximal rate of force rise (MFR) was calculated from the positive-filtered (30-Hz filter frequency) 100-Hz force differential and expressed as a percentage of peak force.² Half relaxation time ($\frac{1}{2}$ Rt) was defined as the time taken for force to decline from 50% to 25% of the peak force. In con-

trast to some other measures of relaxation rate, this measure “normalizes” the data and enables direct comparison of relaxation rates from different absolute levels of tetanic force. The $\frac{1}{2}$ Rt was calculated for all stimulation signals (except 10 Hz) and averaged for each subject. In addition to these standard measures of contractile speed, the relative fusion in response to 10 Hz stimulation was assessed calculating the force oscillation amplitude (FOA) relative to the mean force using the equation:

$$\text{FOA} = dF/F_{\text{mean}} \times 100\%$$

where dF is the average amplitude of three consecutive oscillations in the tetanus after the tension reached its peak and F_{mean} is the mean force during that time (Fig. 2B). Force signals were continuously recorded during the fatigue protocol. The resistance to fatigue of the quadriceps muscle was expressed as

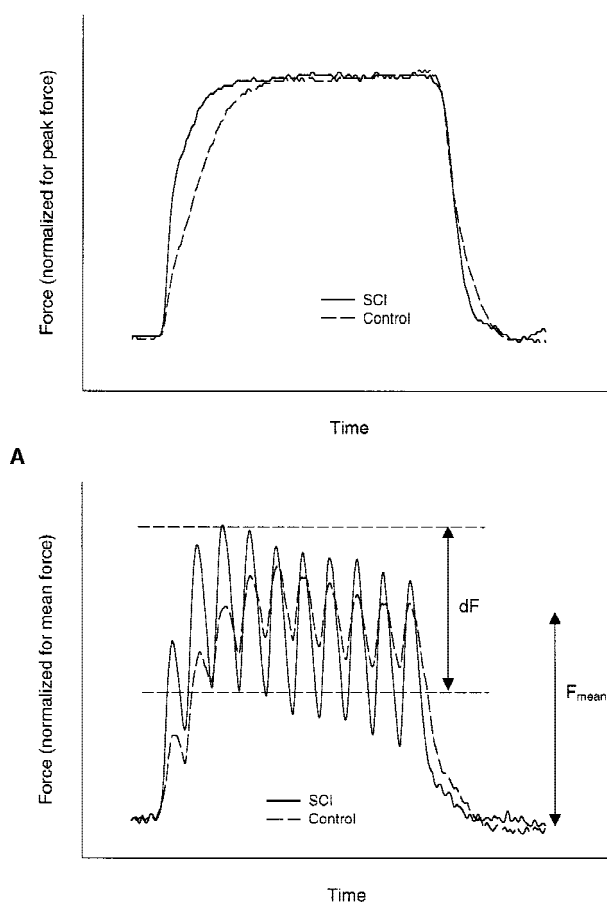


FIGURE 2. Example of typical force responses resulting from 100-Hz (A) and 10-Hz (B) stimulation in SCI (solid line) and control (dashed line) quadriceps muscle. Forces are normalized for mean force in the 10-Hz signal and for peak force in the 100-Hz signal. F_{mean} represents the mean force and dF represents the average amplitude of the oscillations in a 10-Hz signal in SCI (B).

an endurance time, which was defined as the time needed for force to decline to 30% of the prefatigue value.

One of the SCI subjects managed only 2 min before reaching the 30% point and, consequently, comparisons of mean relative forces between groups were made at 2 min of stimulation. In addition, $\frac{1}{2}$ Rt was calculated from the 30-Hz tetani at the start, at 2 min, and at the end of the stimulation protocol.

Statistical Analysis. A two-tailed *t*-test for unequal variances was used to test for differences between control and SCI groups in force–frequency relationships (frequency that generates 50% of 100 Hz force; and 20/50 ratio), contractile speed ($\frac{1}{2}$ Rt; MFR; and FOA) and fatigue (force; and $\frac{1}{2}$ Rt after 2 min). A repeated-measures analysis of variance was used to determine differences in force and relaxation rates at the start, at 2 min, and at the end of the fatigue protocol within each group, and a paired, two-tailed *t*-test was used to test for all differences. We used regression analysis to determine relationships between FOA and force at 2 min of repeated stimulation. All values are described as mean \pm SD, unless otherwise stated, and significance was accepted at levels of 0.05.

RESULTS

Voluntary and Stimulated Force. The MVC force in the control subjects was 746 ± 137 N, and the current needed to produce approximately 30% of this force, using 20 Hz stimulation, was 94 ± 18 mA. The MSC force in the SCI group resulting from 20 Hz tetani was 451 ± 75 N, and the current needed to achieve approximately 30% of this force was 142 ± 25 mA.

Contractile Speed. Figure 2 shows typical force responses in a SCI and a control subject to 100-Hz and 10-Hz stimulation. This figure clearly demonstrates that the SCI quadriceps muscle was characterized by faster contractile properties. Maximal rate of force rise was significantly greater, and $\frac{1}{2}$ Rt was significantly shorter, in SCI compared with control (Table 2) subjects. Low-frequency (10-Hz) stimulation of the quadriceps muscle produced unfused tetani in both control and SCI groups. However, the force oscillations were much greater in SCI compared with control (Table 2) subjects. As is clearly demonstrated in Figure 2B, the force response to 10-Hz stimulation was much less fused in the paralyzed quadriceps muscle than in the nonparalyzed muscle.

Fatigue Characteristics. The force response (expressed as a percentage of the prefatigue force) to

Table 2. Summary of descriptive statistics for MFR (in 100 Hz), $\frac{1}{2}$ Rt (mean of 20 to 100 Hz), and FOA (in 10 Hz) for SCI and control groups.

Variable	SCI (n)	Control (n)	Difference (%) [*]
MFR (%.ms ⁻¹)	$1.46 \pm 0.34^{\dagger}$ (7)	0.96 ± 0.32 (13)	52
$\frac{1}{2}$ Rt (ms)	$29 \pm 3^{\dagger}$ (6)	36 ± 9 (12)	19
FOA (%)	$65 \pm 22^{\dagger}$ (7)	23 ± 8 (13)	183

^{*}Percent of deviation of the SCI values from control values.

[†]Statistical significance for difference between control and SCI groups, *P* < 0.05.

Missing values were due to artifacts in the force signals.

the repeated 30-Hz stimulation declined gradually in both experimental groups (Fig. 3). Force remained above 30% of the prefatigue value throughout the maximal stimulation time of 10 min in all but one of the control subjects (endurance time in that subject was 240 s).

In contrast, the SCI quadriceps muscle was able

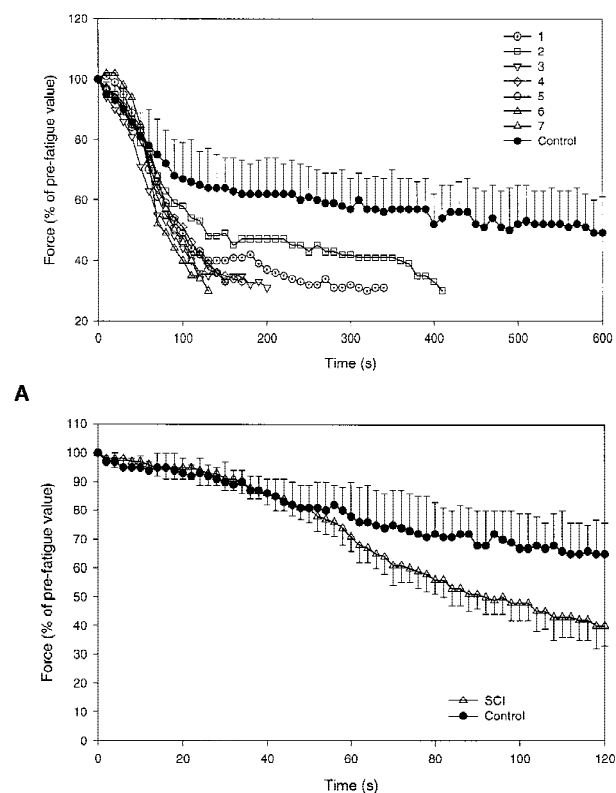


FIGURE 3. Force decline expressed as percent of prefatigue value during the fatigue protocol. **(A)** Force responses are plotted every 10 s during the complete fatigue protocol for each individual SCI subject (1–7) and mean control group (closed circles; *n* = 13). **(B)** Forces are plotted every 2 s during the first 2 min of stimulation for mean SCI (open triangles; *n* = 7) and control group (closed circles; *n* = 13). (Error bars represent SD.)

to maintain force above 30% only for less than 4 min average (mean endurance time, 216 ± 116 s). After 2 min of stimulation, force decline was significantly greater in SCI than in control (Fig. 3B and Table 3): mean force decreased to $41 \pm 7\%$ in SCI and to $65 \pm 10\%$ in control ($P < 0.05$).

In addition to the force decline, $\frac{1}{2}Rt$ was significantly prolonged after 2 min of repetitive quadriceps activation in both SCI and control groups (Table 3). Note, however, the large difference in contractile slowing between the SCI and control groups: $\frac{1}{2}Rt$ increased to $335 \pm 122\%$ of the prefatigue value in SCI, which was significantly greater than control ($160 \pm 34\%$), $P < 0.05$. Interestingly, following the slowing of relaxation in the first 2 min of stimulation, a significant speeding up of relaxation was observed towards the end of the fatigue protocol in the control group (i.e., $\frac{1}{2}Rt$ declined from 57 ± 14 to 47 ± 14 ms, $P < 0.05$). A similar but not significant trend was observed in the SCI group. Despite this recovery of relaxation rate, $\frac{1}{2}Rt$ was still significantly longer at the end of stimulation compared with the start of the fatigue protocol in both control and SCI groups ($131 \pm 34\%$ and $302 \pm 176\%$ of prefatigue value, respectively; $P < 0.05$).

Relationship between Muscle Fatigue and Rate of Fusion in Low-Frequency Stimulation. The relationship between the rate of fusion and fatigue (Fig. 4) was described for the SCI group and the control groups separately. Regression analysis indicated that there was a significant ($P < 0.05$) association between FOA and the percent of prefatigue force after 2 min of repeated stimulation. The correlation was 0.81 in the SCI group and 0.58 in the control group.

Force-Frequency Relationship. The force responses to different stimulation frequencies are presented in Figure 5. The twitch force was calculated from the force response to the first stimulus in the 10-Hz signal. When these forces were normalized for peak force resulting from 100-Hz stimulation, the force-frequency relationship for the SCI group was

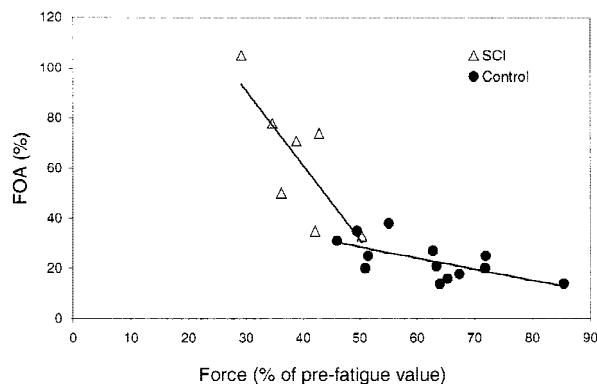


FIGURE 4. Relationship between rate of fusion and fatigability in the SCI (open triangles) and control (closed circles) groups. The FOA is plotted against the percent of prefatigue force after 2 min of repeated 30-Hz stimulation. (See text for correlation coefficients.)

slightly shifted to the left. The SCI group required a significantly lower stimulation frequency to elicit half of maximal 100-Hz force (13 ± 3 Hz) than the control group (16 ± 2 Hz), $P < 0.05$. In addition, the 20/50 ratio was significantly ($P < 0.05$) higher in the SCI group (0.80 ± 0.10) than in the control group (0.69 ± 0.08).

Interestingly, the absolute twitch force in the 10-Hz signal was similar in both SCI and control groups (34 ± 14 N and 34 ± 10 N, respectively), whereas 100-Hz tetanic force was much lower in SCI (192 ± 54 N) than in control (335 ± 68 N), $P < 0.05$. Consequently, when the data are normalized for the 100-Hz tetanic force, the relative twitch force generated by the SCI group is significantly higher ($18 \pm 6\%$) than control ($10 \pm 3\%$), $P < 0.05$.

DISCUSSION

Because the paralyzed muscles of SCI individuals are characterized by a shift in muscle fiber composition towards a predominance of fast glycolytic, type II fibers,^{5,11,19,25,27} high fatigability and concomitant alterations in contractile speed are expected. In contrast with small, distally located muscles, systematic

Table 3. Summary of descriptive statistics for force and $\frac{1}{2}Rt$ of the 30-Hz signal during the repeated stimulation protocol for SCI and control groups.

30 Hz	SCI ($n = 7$)			Control ($n = 12$)		
	t_0	t_2	t_{end}	t_0	t_2	t_{end}
Force (N)	143 ± 40	$58 \pm 24^*$	$45 \pm 15^{*†}$	260 ± 51	$160 \pm 38^*$	$122 \pm 40^{*†}$
$\frac{1}{2}Rt$ (ms)	31 ± 8	$98 \pm 20^*$	$84 \pm 21^*$	37 ± 9	$57 \pm 14^*$	$47 \pm 14^{*†}$

*Statistical significance of difference from prefatigue value (t_0).

†Statistical significant difference between levels after 2 min (t_2) and at the end of stimulation (t_{end}), $P < 0.05$.

Missing values were due to artifacts in the force signals.

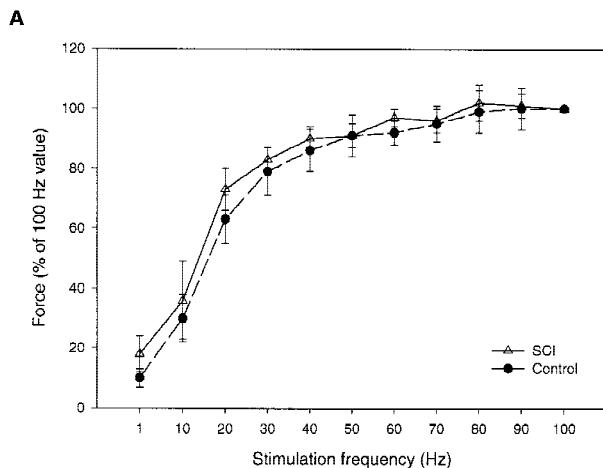
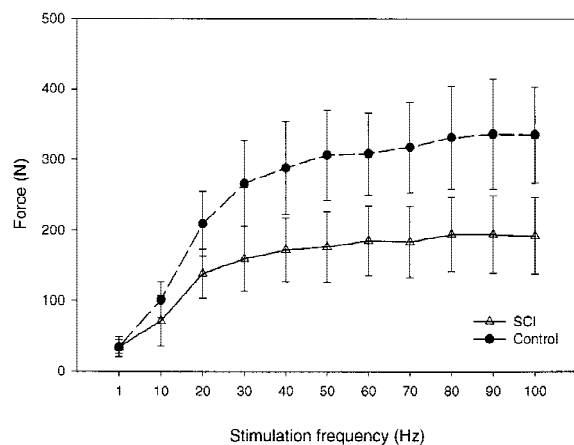


FIGURE 5. Force–frequency relationship in SCI (open triangles on solid line; $n = 7$) and control (closed circles on dashed line; $n = 13$) quadriceps muscle. Force responses to different stimulation frequencies are given in absolute forces (**A**) and normalized for peak isometric 100-Hz force (**B**). (Error bars represent SD.)

data regarding the physiological properties of the large, paralyzed quadriceps muscle is limited. In this study, we have investigated selected contractile properties as well as fatigability of the quadriceps muscle in SCI and able-bodied control individuals.

The gender composition differed between our two groups of subjects. It is known that there exist differences between men and women subjects regarding muscle mass and force. There is, however, no evidence of systematic differences in muscle fiber composition or contractile properties. In the present study, no significant differences were seen between the men and women control subjects regarding the contractile properties or fatigability. Therefore, the data for men and women subjects have been amalgamated in each group.

All isometric force measurements for the determination of contractile properties and fatigability

were carried out using a stimulation intensity that produced approximately 30% of maximal muscle force. It is generally known that during a MVC, a healthy person is able to maximally activate the muscle, provided that the subject is well instructed and trained to perform a MVC. The control subjects in the present study were all well instructed and showed only little variation between the three consecutive MVCs, and we therefore believe that the subjects were able to maximally activate their quadriceps.

When the muscles of the SCI subjects were stimulated with increasing current, the force started to level off at a certain current intensity. We assumed that this was the point at which the entire muscle was activated. Consequently, the current required to produce 30% of the MVC (in controls) and 30% of the MSC (in SCI) could be determined and compared.

It should be noted that this stimulation intensity was markedly higher in the SCI group (142 ± 25 mA) than in the control group (94 ± 18 mA). The higher current required in the SCI muscles may be due to an increase in the amount of subcutaneous fat or large amounts of perimysial tissue.²¹ It might be noted, however, that Cope et al.⁷ reported that motoneurons in chronic spinally transected cats were less electrically excitable, and the authors suggested that this may be a general response of extensor motoneurons following chronic spinal cord transection.

Contraction/Relaxation Speed. In the present study, the MFR was about 50% faster, and $\frac{1}{2}Rt$ about 20% shorter in the paralyzed quadriceps muscle compared with the normal control muscle. These results confirm the findings in the smaller, more distally located tibialis anterior^{26,33} or soleus muscles.^{29,30} Moreover, these alterations in contractile properties following SCI appear to be well matched to the histochemical findings of an increased proportion of type II muscle fibers determined from muscle biopsies.^{25,26} Although biopsies of the quadriceps muscles have not been undertaken in the present study, a shift towards faster histochemical characteristics in this muscle has been well documented in previous literature.^{5,11,27}

This fiber type transformation seems to commence within weeks postinjury,⁵ suggesting that the paralyzed muscles of the SCI subjects in the present study probably had a predominance of type II muscle fibers. We therefore suggest that our results of increased contractile speed reflect the expected histochemical alterations in muscle fiber composition.

Fatigue. The muscles of the SCI individuals fatigued much more rapidly than did the control muscles, characterized by a greater force decline and an augmented prolongation of relaxation. These results support the findings of previous studies, which reported an impaired endurance capacity.^{23,24,29,30,33} The marked increase in muscle fatigability following spinal cord transection is a well-recognized sequela to the loss of descending activation and the consequent transformation of the muscle fibers towards type II fibers. These fast-twitch fibers have a high glycolytic and low oxidative capacity and are known to fatigue more readily than do the slow-twitch (type I) fibers.^{4,9}

An important additional factor enhancing rapid fatigue in the SCI muscles may be impaired muscle blood flow, which would limit oxygen and energy supply to the exercising muscle and allow accumulation of potassium and metabolic products such as lactate and inorganic phosphate. In able-bodied individuals, repeated isometric contractions reduce muscle blood flow,³² but this effect may be more pronounced in the paralyzed limbs of SCI subjects as a result of an impaired vascular capacity¹³ and reduced blood flow in the femoral artery.¹⁴ Indeed, this may underlie the observation of Pilegaard et al.,²² who reported a lower sarcolemmal lactate/H⁺ transport capacity in the thigh muscle of SCI subjects than in able-bodied untrained subjects.

Interestingly, the slowing of relaxation as a result of repeated stimulation did not follow a steady progression throughout the fatigue protocol. In the control group, the rate of relaxation at the end of the 10-min fatigue protocol was faster compared with the values after 2 min. This recovery of relaxation speed may result from a restoration of muscle blood flow or a subsequent rise in muscle temperature as exercise proceeds.

Rate of Fusion in 10-Hz Response. The difference between the SCI and control groups in the rate of tetanic fusion of the 10-Hz signal was very pronounced: the relative amplitudes of the force oscillations in the SCI group were almost 200% higher than in the control group. This dramatic difference may result from both augmented contraction and relaxation speed, but other muscle characteristics, such as the increased twitch height, may further amplify the force oscillations.

The large variability in rate of fusion in the SCI subjects in our study may reflect variability in the number of fast-twitch fibers as a result of differences in the duration of the spinal lesion. It has previously been shown that the degree of type I to type II trans-

formation is related to lesion duration.³ The close correlation between FOA and fatigue suggests that in the SCI subjects, the enhanced fatigue indeed largely depends on the number of type II muscle fibers. In contrast, the control group was characterized by a small variability in FOA and greater variability in fatigue. Moreover, the correlation between FOA and fatigue was weaker in this group, suggesting that muscular fatigue in normal, able-bodied muscle is less determined by the fiber type composition than by other factors, such as blood flow or central regulation of blood pressure.

Force-Frequency Response. At low-stimulation frequencies within the physiological range, fast muscles generate less force than do slow muscles, as described by the force-frequency relationship. This relationship can be characterized by determining the stimulation frequency required to elicit a set proportion of tetanic force⁶ (50% in the present study).

Another method is to express the forces generated at low frequencies as a proportion of forces at high frequencies (in this study, we calculated the ratio of 20-Hz and 50-Hz forces). The present study clearly showed that the SCI muscles exhibited a force-frequency relationship that might be expected for a muscle that was slower than normal in able-bodied individuals. This paradoxical finding was also previously reported by Rochester et al.²⁶ in a study of human paralyzed tibialis anterior muscle.

Clearly, a shift to the left of a force-frequency relationship could have been due either to an impaired high-frequency response or an augmented low-frequency response, or a combination of both. Although long-term loss of descending activation may lead to an impairment of excitation-contraction coupling at high-stimulation frequencies, we have no direct evidence to confirm this. On the other hand, it is notable that the absolute twitch force is the same in both SCI and control groups, despite a reduction in tetanic force by approximately 40% (Fig. 5A). Moreover, when the data are normalized for the 100-Hz tetanic force, the relative twitch force generated by the SCI group is almost twice that generated by the control group (Fig. 5B). We have no explanation for the elevated twitch force, but it most likely determines the relatively high forces at low-stimulation frequencies, shifting the force-frequency relationship to the left (Fig. 5B).

A similar unexplained increase in twitch force has been reported following denervation of mammalian skeletal muscle,^{1,12} which may have the same origin. From a practical viewpoint, the present data clearly show that the force-frequency response is not

a reliable guide to the known changes in muscle contractile speed or muscle fiber composition following SCI.

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